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## BRAIN RESEARCH

# **Optimizing estimation of hemispheric dominance for language using magnetic source imaging**

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#### ABSTRACT

The efficacy of magnetoencephalography (MEG) as an alternative to invasive methods for investigating the cortical representation of language has been explored in several studies. Recently, studies comparing MEG to the gold standard Wada procedure have found inconsistent and often less-than accurate estimates of laterality across various MEG studies. Here we attempted to address this issue among normal right-handed adults (N=12) by supplementing a well-established MEG protocol involving word recognition and the single dipole method with a sentence comprehension task and a beamformer approach localizing neural oscillations. Beamformer analysis of word recognition and sentence comprehension tasks revealed a desynchronization in the 10-18 Hz range, localized to the temporo-parietal cortices. Inspection of individual profiles of localized desynchronization (10-18 Hz) revealed left hemispheric dominance in 91.7% and 83.3% of individuals during the word recognition and sentence comprehension tasks, respectively. In contrast, single dipole analysis yielded lower estimates, such that activity in temporal language regions was left-lateralized in 66.7% and 58.3% of individuals during word recognition and sentence comprehension, respectively. The results obtained from the word recognition task and localization of oscillatory activity using a beamformer appear to be in line with general estimates of left hemispheric dominance for language in normal right-handed individuals. Furthermore, the current findings support the growing notion that changes in neural oscillations underlie critical components of linguistic processing.

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#### 1. Introduction

The utility of magnetoencephalography (MEG) as an alternative to traditional invasive methods for the study of the cortical representation of language has been explored in several studies which differ in their experimental design and analytical approach. Using a verbal continuous recognition memory (CRM) protocol, we have previously reported on the cardinal features of MEG-derived cortical activation maps for receptive language, marked by a greater degree of activity in the left temporo-parietal cortex (including the posterior portions of the middle and superior temporal gyri; and the supramarginal and angular gyri) (Breier et al., 1999, 2000; Papanicolaou et al., 1999). Moreover, the efficacy of this protocol in assessing hemispheric dominance for language has been addressed in studies involving brain surgery

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candidates, the largest of which demonstrated a high degree of concordance (87%) between language laterality judgments made on the basis of MEG mapping and those made, independently, on the basis of the Wada procedure which involves anesthetization of each hemisphere while assessing language and which constitutes the "gold standard" (Papanicolaou et al., 2004).

In addition to the CRM protocol, studies employing alternative language tasks and source modeling techniques have also reported on the efficacy of MEG as a non-invasive means for establishing hemispheric dominance for language, with some degree of variability on laterality estimates among them. In an early study comparing MEG findings to the Wada, Szymanski et al. (2001) found 71% of right-handed tumor patients to be leftlateralized for language using the single dipole method of analysis. Some years later, Bowyer et al. (2004) found a higher level of concordance (89%) between MEG and Wada results among 27 epilepsy patients using a source density-imaging technique. In a later study by Kamada et al. (2007), MEG and fMRI-based laterality judgments from 87 patients with brain lesions were matched to Wada findings in 100% of the cases. However, the analysis used in this study and the subsequent level of agreement with the Wada would not have been possible using only one imaging modality. Even still, this study suggests that across a large sample, establishing language laterality noninvasively is possible. More recent studies have dissected the MEG signal into time-frequency components and utilized a beamformer to estimate the corresponding sources of activity. For example, Kim and Chung (2008) correctly established language laterality compared to the Wada procedure in 12 out of 17 (71%) epilepsy patients based on localization of activity in the left temporal-parietal cortex, employing an auditory verbal oddball paradigm and a spatial filtering method. Furthermore, using the posterior aspect of the inferior frontal gyrus (IFG) for the region of interest (ROI), the latter study demonstrated that correct laterality judgments were made in 94% (16 out of 17) of the cases studied. Similarly, Hirata et al. (2010) recently found an 85% degree of concordance between Wada and MEG-derived measures of laterality in the IFG, middle frontal gyrus (MFG), and the insular cortex, utilizing a silent word reading task and a beamformer among 60 patients. While MEG estimates of language dominance appear to be improving, there exists variability across the results of language studies published over the last decade due to differences in data analysis techniques and experimental paradigms.

In the majority of clinical studies, estimates of laterality based on non-invasive neuroimaging methods result in a smaller percentage of left-hemisphere (LH) dominance than would be expected. This may be due to the fact that among patients, particularly candidates for epilepsy surgery, interhemispheric dominance shift resulting in more right hemisphere dominant patients is likely to occur (Pataraia et al., 2004, 2005). But this does not account for the lower percentage of LH dominance found using MEG compared to that found with the Wada procedure in the same patient group (Papanicolaou et al., 2004). Therefore, this marginal underestimation of the percentage of LH dominant cases found with MEG may be due to either the task or to the analysis procedure used. Accordingly, in this study we explored the possibility that more accurate laterality estimates could be derived by introducing a more naturalistic language activation task in conjunction with an alternative MEG analysis procedure to the one we are typically employing, with a sample of right-handed normal individuals. However, in order to assess the possible improvements associated with alternative task and analysis techniques, we must first adopt an independent and valid estimate of left-hemisphere dominance in the normal population as a guideline for our study.

In the general population, it has long been estimated that roughly 96% of right-handed individuals are left-dominant for language on the basis of a large sample of epilepsy patients (Rasmussen and Milner, 1977). While this estimate is often cited to explain language dominance in the normal population, a more realistic estimate may be derived by studying individuals with language impairment due to acute unilateral brain injury. Among these patients, the possibility of lesion-induced hemispheric dominance shift is eliminated. In a recent study by Moser et al. (2011), several large-scale studies were identified which reported on unilateral stroke resulting in aphasia. On the basis of these studies, they concluded that approximately 90% of normal individuals are left-lateralized for language regardless of handedness. Furthermore, when the proportion of left- and righthanded individuals in the general population is considered, the percentage of left-lateralized individuals rises to 94% among right-handed people. Accordingly, this percentage may serve as a more accurate estimate of hemispheric dominance for language among the general population.

In addition to clinical populations, hemispheric dominance for language has been studied with noninvasive functional imaging methods among neurologically intact individuals as well. For example, in a large-scale normative MEG study by Papanicolaou et al. (2006) using the single-word CRM paradigm and an automated dipole localization technique, it was found that hemispheric dominance for receptive language is mainly accounted for by sustained activity in the left middle temporal gyrus, a finding which did not vary as a function of age, gender or stimulus modality. Moreover, using a variant of the CRM paradigm, Mohamed et al. (2008) localized language-specific event-related desynchronization (ERD) to a region in the posterior superior temporal gyrus (STG) of the left hemisphere using a small normative sample. In addition, Cornelissen et al. (2009) used a passive word reading task and a similar analysis technique with a sample of healthy controls and found a preponderance of activation in the left posterior STG region. However, the aforementioned studies reported group averages and did not specify estimates of hemispheric dominance for each individual subject. Therefore, in this study we attempted to directly address this issue on a case-by-case basis by supplementing the well established CRM paradigm and the equivalent current dipole analysis with an alternative language task involving sentence comprehension and a source analysis involving time frequency (TF) and beamformer methods.

#### 2. Results and discussion

#### 2.1. In-scanner task performance

Percent correct identification of targets was 95.1%±2.3 for the CRM task, demonstrating excellent accuracy across

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